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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,786	02/20/2004	David M. Kranz	89-99A	7830
23713 7590 12/14/2007 GREENLEE WINNER AND SULLIVAN P C 4875 PEARL EAST CIRCLE SUITE 200 BOULDER, CO 80301			EXAMINER GUZO, DAVID	
			ART UNIT	PAPER NUMBER
			1636	
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			12/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/783,786

Applicant(s)

KRANZ ET AL.

Examiner

David Guzo

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 9/26/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-26,28-34 and 36-83 is/are pending in the application.
- 4a) Of the above claim(s) 11-24,38-49 and 56-81 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6-10,33,34,36,37,82 and 83 is/are allowed.
- 6) ☒ Claim(s) 1,4,25,26,28-32 and 50-55 is/are rejected.
- 7) ☒ Claim(s) 2 and 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 6/14/07.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

Detailed Action

Election/Restriction

Claims 11-24, 38-49 and 56-81 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/10/07.

Priority

Priority for the claimed invention is granted back to the filing date of the 60/169,179 provisional application (12/06/1999).

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4, 54 and 55 are rejected under 35 U.S.C. 102(a) as being anticipated by Manning et al.

Applicants claim a method for using high affinity TCRs to identify ligands comprising: labeling high affinity TCRs; contacting said labeled TCRs with peptide/MHC ligands; identifying the ligand with which the labeled TCR is bound. Applicants also claim a method of using high affinity TCRs to bind to a selected peptide/MHC ligand

comprising: labeling said high affinity TCRs with a label that binds to the selected peptide/MHC ligand with a label; contacting said labeled high affinity TCRs with cells containing MHC molecules. Applicants also claim a method of binding a high affinity TCR to a cell carrying a selected peptide/MHC ligand on the cell surface which comprises the steps of: providing a mutant TCR having high affinity for the selected peptide/MHC complex and carrying one or more mutations in a CDR (can be in CDR3 α or CDR3 β); labeling the high affinity TCR; contacting the labeled high affinity TCRs with a sample containing cells carrying one or more peptide/MHC ligands on the cell surface to bind the high affinity TCRs to selected peptide/MHC ligands present in the sample.

It is noted that applicants define a "high affinity TCR" as an engineered TCR with stronger binding to a target ligand than the wild-type TCR.

Manning et al. (cited by applicants, J. Exp. Med., Vol. 189, Feb. 1, 1999, pp. 461-470, see whole article, particularly the Abstract, right column on p. 462, Figs. 2-3, etc.) teaches labeling high affinity TCRs (the mutant high affinity TCRs are labeled with a HIS tag, added during generation and purification of the scTCRs) comprising mutations in CDR3 α wherein said mutant TCRs have a higher binding affinity for a target pMHC. The labeled high affinity TCRs are contacted with cells comprising the pMHC ligands on their surfaces wherein the ligands are identified. Manning et al. therefore teaches the claimed invention.

35 USC 112, 1st Paragraph Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26, 28-32 and 50-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record in the previous Office Action (mailed 3/26/07) and for reasons outlined below.

Applicants traverse this rejection by asserting that the skilled artisan could envision a representative number of species which describe the claimed genus. Applicants assert that the state of the art in binding assays is well developed and applicants assert that the detailed description provided in the specification shows a binding affinity assay in which soluble TCRs are used at varying concentrations to measure the binding affinity of the interaction with its cognate peptide/MHC (QL9/Ld). Applicants cite prior art (already of record) concerning assays to measure affinities of TCR:pepMHC interactions and assert that:

While the affinities of the TCRs measured prior to this application were for wild type TCRs, it is well known in the fields of biochemistry and immunology that proteins (e.g. TCRs) with affinities in the higher affinity range of 10^7 M^{-1} to 10^{10} M^{-1} would be even easier to measure by the standard techniques known in the art. This fact stems most directly from two properties of higher affinity interactions: the need for less soluble protein when affinities are higher, and the reduced non-specific interactions that occur at these lower protein concentrations. These factors are well known in the art.

Applicant's arguments filed 9/26/07 have been fully considered but they are not persuasive. Applicants appear to be arguing that since the prior art and instant specification enable the identification of high affinity TCRs with the claimed binding characteristics, the claimed TCRs are described. In response, the examiner notes that the written description requirement is distinct from the enablement requirement of 35 USC 112, 1st paragraph, see MPEP 2161:

The written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), *cert. denied*, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991) (While acknowledging that some of its cases concerning the written description requirement and the enablement requirement are confusing, the Federal Circuit reaffirmed that under 35 U.S.C. 112, first paragraph, the written description requirement is separate and distinct from the enablement requirement and gave an example thereof.). An invention may be described without the disclosure being enabling (e.g., a chemical compound for which there is no disclosed or apparent method of making), and a disclosure could be enabling without describing the invention (e.g., a specification describing a method of making and using a paint composition made of functionally defined ingredients within broad ranges would be enabling for formulation falling within the description but would not describe any specific formulation).

Applicants appear to be asserting that since the specification and prior art teaches assays for measuring the binding affinity between TCRs with their cognate ligands, the skilled artisan could easily "envision" a representative number of species which describe the claimed genus. This argument is not persuasive because neither the instant disclosure nor the prior art teaches any of the structural features of the claimed high affinity TCRs which would distinguish them from the wild-type TCRs from which they are derived or indeed, from any other TCRs. Merely claiming high affinity TCRs by function only (with certain dissociation constants) without a structure-function

relationship does not satisfy the written description requirement in this case. A definition of the TCRs by function does not suffice to describe the genus because it is only an indication of what the TCR does rather than what it is (See *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)).

Also, the prior art does not provide any examples of high affinity TCRs which exhibit dissociation constants for the pMHC ligands greater than about 10^7 M^{-1} . Indeed, Manning et al. (cited above) notes that the highest affinities for any TCR-pMHC interactions yet measured have been $K_d = 10^{-7} \text{ M}$. The prior art therefore cannot provide a description of high affinity TCRs with dissociation constants greater than 10^7 M^{-1} and the skilled artisan would be unable to envision TCRs with the recited dissociation constants. The rejection therefore stands.

Any rejections not repeated in this Office Action are withdrawn.

Claims 6-10, 33-34, 36-37, 82 and 83 are allowed.

Claims 2 and 5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571)

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272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


DAVID GUZO
PRIMARY EXAMINER

David Guzo
December 5, 2007